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TITLE : NOSE CLEANING AGENT

ABSTRACT : PURPOSE: To obtain a nose cleaning agent of an O/W emulsion capable of controlling invasion of allergen of pollinosis, etc.

CONSTITUTION: 1-50wt.% of an oil component (e.g. middle-chain fatty acid triglyceride) is properly mixed with 0.05-5wt.% of a surfactant, water, a pH adjustor and components useful for an ordinary nasal drop, adjusted to pH 3.5-5.5 and pharmaceutically manufactured into a milky O/W type emulsion to give a nose cleaning agent. Elution of allergen from pollen particles having entered a nasal cavity is subdued by keeping pH in a nasal cavity weakly acidic by spraying the nose cleaning agent from a nasal drop container and movement of allergen substance to the interior of nasal mucosa can be suppressed by forming an oil film on the surface of a nasal mucosa. The nose cleaning agent has higher allergen washing action than a conventional nose cleaning agent by raising pH.

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Industrial Application] About the rhinenchysis agent which consists of an O/W mold emulsion of pH 3.5-5.5, this invention forms an oil film layer after spraying and in a nasal cavity from a rhinenchysis container, maintains pH of the front face of the tunica mucosa nasi at a weak acidic condition, and relates to the rhinenchysis agent which controls invasion of allergen, such as pollen.
[0002]
[Description of the Prior Art] By the increment in a hay fever sufferer, the need of the rhinenchysis agent aiming at washing in a nasal cavity of the pollen which invaded in the nasal cavity is increasing quickly in recent years. Generally the extract of the allergen from a pollen particle is performed under an alkaline solution. Moreover, pH in the nasal allergy patient's nasal cavity is called 7.8-8.5. The pollen particle which thought from the onset.device of allergy, for example, invaded in the nasal cavity is eluted in the protein which serves as a basis of allergy under alkaline conditions, invades through the tunica mucosa nasi in the living body, and causes an allergy symptom (a sneeze, a runny nose, nasal congestion) by the antigen-antibody reaction.
[0003] The thing neutral in pH of pharmaceutical preparation or alkaline of the conventional rhinenchysis agent is main. When this makes pH high, it is the purpose to extract and flush allergen from a pollen particle. However, in the conventional rhinenchysis agent, the operation which flushes allergen was not enough, therefore there was a fault that an allergy symptom was caused by the allergen which remained. The purpose of this invention is to offer the high rhinenchysis agent of effectiveness to pollinosis etc. in such a situation.
[0004]
[Means for Solving the Problem] By this invention persons' pressing down the elution of the allergen from the pollen particle which advanced into the nasal cavity by maintaining pH in a nasal cavity at the acescence as a result of advancing research wholeheartedly, and pressing down shift of the allergen matter inside the tunica mucosa nasi by making an oil film form on the surface of the tunica mucosa nasi further, it found out that said purpose could be attained and this invention was completed. That is, this invention is a rhinenchysis agent which consists of an O/W mold emulsion of pH 3.5-5.5.
[0005] In this invention, in order to prepare an O/W mold emulsion, an oil component (1-50, preferably 20 - 40 % of the weight), a surfactant (0.05 to 5.0, preferably 0.1 - 3.0 % of the weight), and water are used. The thing liquefied as said oil component, the solid thing, or thing of a half-solid can mention jojoba oil, a sasanqua oil, an avocado oil, soybean oil, olive oil, safflower oil, Oenotherae Biennis oil, corn oil, high-class polyhydric alcohol, a fatty acid, a medium-chain-fatty-acid triglyceride, fatty acid ester, squalene, etc. to water that what is necessary is just insolubility.

Among these, the oil components (soybean oil, medium-chain-fatty-acid triglyceride, etc.) which will be in a distributed condition with a surface active agent, lecithin, etc. are desirable. As said surfactant, although any of a nonionic surfactant, a cationic surfactant, an anionic detergent, an amphoteric surface active agent, and amphiphile are sufficient, the nonionic surfactant or amphiphile usually used for a rhinenchysis agent from the field of safety is desirable. For example, even if it can mention a sorbitan fatty acid ester, a glycerine fatty acid ester, polyethylene glycol fatty acid ester, polyoxyethylene alkyl ether, polyoxyethylene hydrogenated castor oil, polyoxyethylene sorbitan fatty acid ester, a sodium N-acyl methyl taurate salt, an imidazolium betaine, and phospholipid (lecithin, such as phospholipid which hydrogenated natural phospholipid, synthetic phospholipid, and natural phospholipid) and uses one sort independently among these, it does not matter even if two or more sorts are mixed and it uses.

[0006] Although pH regulator is used in order to set pH of pharmaceutical preparation to 3.5-5.5, a hydrochloric acid, a phosphate buffer solution, etc. can be mentioned as a pH regulator.

[0007] The rhinenchysis agent of this invention can blend the matter (dibucaine hydrochloride, lidocaine, lidocaine hydrochloride, procaine hydrochloride, etc.) usually used for the nasal drop other than an oil component, a surfactant, and pH regulator, for example, local anesthetic, germicides (Hibitane, a benzalkonium chloride, dequalinium chloride, etc.), anti-inflammatory agents (glycyrrhizic acid, vitamin C, etc.), thickeners (a polyvinyl pyrrolidone, methyl cellulose, hydroxypropylcellulose, etc.), isotonizing agents (glycerol etc.), a stabilizing agent, a cool-ized agent, etc. in the range which does not spoil the effectiveness of this invention.

[0008] The rhinenchysis agent of this invention can be prepared as follows, for example. That is, the aqueous phase which added germicides (benzethonium chloride etc.) etc. is added to the oil phase containing an oil component and a surface-active-agent component, and it agitates to it violently, and prepares to it according to the usual emulsification method, and pH of the last pharmaceutical preparation is adjusted to it 3.5-5.5. The O/W mold emulsion of stable opalescence is obtained by preparing by powerful shearing force, such as a homomixer, MANTON gaulin, and an ultrasonic emulsifier, in that case.

[0009]

[Effect of the Invention] This invention enabled it to offer the high rhinenchysis agent of effectiveness to pollinosis etc.

[0010]

[Example] An example and the example of a trial are shown below, and this invention is further explained to a detail.

The example 1 (manifestation trial of the nasal allergy symptom by the rhinenchysis agent) of a trial

[Preparation of a sample]

Sample 1: 0.02 % of the weight of benzethonium chloride, vitamin C 0.5% of the weight, melt 1.5 % of the weight of glycerols to purified water, and carry out churning mixing, the thing which made the surface active agent dissolve HCO-60 (trade name of polyoxyethylene hydrogenated castor oil 60) 0.2 % of the weight and RESHINORU S-10 (trade name of hydrogenation soybean lecithin) 0.5 % of the weight to PANASETO 810 (trade name of medium-chain-fatty-acid triglyceride) 20% of the weight is made to emulsify, the dilute hydrochloric acid of pH regulator is set to pH4 of ** for optimum dose, and pharmaceutical preparation, and it ****s in the

100g of whole quantity.
Sample 2: Phosphate buffer solution (pH7.8).
[0011] [Test method] An oral consultation was given about 15 23-42-year-old allergic rhinitis patients, and it checked that it was pollinosis. The duration of test could be two weeks. It divided into two groups of A; 8 persons and B; 7 persons, and one week of the start did not perform nasal cavity washing, but followup of the symptom only by the nasal drop was performed. the following one week -- A group; -- a sample 1 and B group; -- spraying administration of the sample 2 was carried out by a unit of 2 times before the time of going home, and sleeping after lunch at both nasal cavities at the time of morning rising. The judgment according extent of the allergy symptom on the 1st to self-assessment was performed, and the symptom log vote was filled in. Throughout [trial term] stopped use of the sinus medication by oral administration. Moreover, concomitant use of the commercial collunarium was accepted if needed for a symptom. I had the use count of the rhinenchysis indicated on a case card in that case.
[0012] A [result] result is shown in Table 1 and 2. By A group, what has the slight symptom of rhinitis was observed at the 2nd week as compared with B group. Moreover, mitigation was accepted also in the use count of the collunarium a little.
[0013]
[Table 1]

年齢	性	観察日 第1週目													
		1日目		2日目		3日目		4日目		5日目		6日目		7日目	
		程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数
A群															
23	女	++	13	++	10	+++	15	++	7	++	10	++	15	+++	15
25	女	++	14	++	12	++	11	++	13	+++	16	++	10	++	12
26	男	++	7	++	6	++	8	++	8	++	8	++	7	++	6
27	女	++	5	++	5	+	4	+	6	+	7	+	8	++	10
28	男	+	6	+	6	+	6	+	6	+	7	+	8	+	7
28	男	++	7	+	7	+	8	++	10	++	10	+	7	+	6
36	男	++	10	++	10	+++	13	+++	14	++	12	++	10	+++	13
42	男	++	7	++	9	++	8	++	8	++	8	++	10	+	6
B群															
24	男	++	15	+++	15	++	10	++	12	+++	13	+++	10	+++	14
24	女	+	8	+	9	+	7	+	5	++	13	+	8	++	15
26	女	++	15	+++	20	++	18	+++	22	+++	20	+++	23	+++	20
27	女	+	7	+	7	+	8	+	6	+	7	+	5	+	7
29	男	++	10	++	8	+	9	+++	11	+++	11	+++	12	+++	14
33	男	++	10	++	7	++	8	+	5	+	10	++	10	++	13
36	男	++	11	++	11	++	11	++	9	++	8	++	10	++	15

症状の程度：4段階

高　度（非常に悪い）：+++
中等度（　　悪い）：++
軽度　（　やや悪い）：+
なし　（　　良好）：−

[0014]
[Table 2]

年齢	性	観察日 第2週目													
		1日目		2日目		3日目		4日目		5日目		6日目		7日目	
		程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数
A群															
23	女	++	7	+	5	++	6	+	5	+	6	++	9	+	7
25	女	++	8	+	4	+	5	++	5	+	5	++	7	++	6
26	男	++	7	+	5	+	5	++	6	++	6	++	5	++	5
27	女	++	5	++	5	+	4	+	4	++	5	+	4	+	5
28	男	+	6	+	6	+	6	+	5	+	4	+	4	+	5
28	男	++	7	++	8	++	7	+	6	+	6	++	7	++	7
36	男	++	10	++	10	++	10	++	8	++	10	++	11	++	10
42	男	++	8	++	7	++	7	+	6	+	6	+	5	+	6
B群															
24	男	++	10	++	12	+++	13	++	11	++	9	++	8	+++	13
24	女	++	10	+	5	+	8	++	11	++	12	++	10	++	10
26	女	+++	20	+++	25	+++	18	+++	18	+++	20	+++	20	+++	18
27	女	+	7	+	5	++	10	+	6	+	4	++	8	+	4
29	男	++	10	++	8	+++	14	+++	14	++	10	++	8	++	6
33	男	++	8	++	7	++	10	+++	15	+++	15	++	10	++	10
36	男	++	8	++	10	++	10	++	10	+++	15	++	10	+	9

症状の程度：4段階

高　度（非常に悪い）：+++

中等度（　　悪い）：++

軽度　（　やや悪い）：+

なし　（　　良好）：−

[0015] Example 1 Component Loadings (% of the weight)
Benzethonium chloride 0.02 PANASETO 810 30 RESHINORU S-10 0.5 Glycerol 2 L-menthol 0.05 Dilute hydrochloric acid Optimum dose (pharmaceutical preparation pH 4.5)
Purified water All 100g benzethonium chloride and a glycerol were melted to purified water, and the rhinenchysis agent was prepared by carrying out churning mixing, making what dissolved HCO-60, RESHINORU S-10, and l-menthol in PANASETO 810 emulsify, setting dilute hydrochloric acid to pH4 of ** for optimum dose, and pharmaceutical preparation, and considering as 100g of whole quantity.
[0016] Example 2 Component Loadings (% of the weight)
Lidocaine 0.1 Benzethonium chloride 0.02 PANASETO 810 10 HCO-60 0.2 RESHINORU S-10 0.3 Glycerol 1.5 Hydroxymethyl cellulose 0.02 Phosphate buffer solution A total (pharmaceutical preparation pH 3.5) of 100g
The rhinenchysis agent was substantially prepared similarly with the example 1.
[0017] Example 3 Component Loadings (% of the weight)
Cetylpyridinium chloride 0.02 Soybean oil 20 Tween80 0.2 RESHINORU S-10 0.5 Glycerol 1.0 Dilute hydrochloric acid Optimum dose (pharmaceutical preparation pH 5.0)

Purified water The rhinenchysis agent was substantially prepared similarly with all the 100g examples 1.
[0018] Example 4 Component Loadings (% of the weight)
Glycyrrhizinate dipotassium 0.5 Benzethonium chloride 0.02 PANASETO 810 10 HCO-60 0.2 RESHINORU S-10 0.3 Glycerol 1.5 Hydroxymethyl cellulose 0.01 Dilute hydrochloric acid Optimum dose (pharmaceutical preparation pH 4.0) Purified water The rhinenchysis agent was substantially prepared similarly with all the 100g examples 1.
[0019] Example 5 Component Loadings (% of the weight)
Benzalkonium chloride 0.02 PANASETO 810 30 Pre SOMU 0.5 Glycerol 1.5 Phosphate buffer solution A total (pharmaceutical preparation pH 4.0) of 100g The rhinenchysis agent was substantially prepared similarly with the example 1.

TECHNICAL FIELD

[Industrial Application] About the rhinenchysis agent which consists of an O/W mold emulsion of pH 3.5-5.5, this invention forms an oil film layer after spraying and in a nasal cavity from a rhinenchysis container, maintains pH of the front face of the tunica mucosa nasi at a weak acidic condition, and relates to the rhinenchysis agent which controls invasion of allergen, such as pollen.

EFFECT OF THE INVENTION

[Effect of the Invention] This invention enabled it to offer the high rhinenchysis agent of effectiveness to pollinosis etc.

TECHNICAL PROBLEM

[Description of the Prior Art] By the increment in a hay fever sufferer, the need of the rhinenchysis agent aiming at washing in a nasal cavity of the pollen which invaded in the nasal cavity is increasing quickly in recent years. Generally the extract of the allergen from a pollen particle is performed under an alkaline solution. Moreover, pH in the nasal allergy patient's nasal cavity is called 7.8-8.5. The pollen particle which thought from the onset device of allergy, for example, invaded in the nasal cavity is eluted in the protein which serves as a basis of allergy under alkaline conditions, invades through the tunica mucosa nasi in the living body, and causes an allergy symptom (a sneeze, a runny nose, nasal congestion) by the antigen-antibody reaction.
[0003] The thing neutral in pH of pharmaceutical preparation or alkaline of the conventional rhinenchysis agent is main. When this makes pH high, it is the purpose to extract and flush allergen from a pollen particle. However, in the conventional rhinenchysis agent, the operation which flushes allergen was not enough, therefore there was a fault that an allergy symptom was caused by the allergen which remained. The purpose of this invention is to offer the high rhinenchysis agent of effectiveness to pollinosis etc. in such a situation.

MEANS

[Means for Solving the Problem] By this invention persons' pressing down the elution of the allergen from the pollen particle which advanced into the nasal cavity by maintaining pH in a nasal cavity at the acescence as a result of advancing research wholeheartedly, and pressing down shift of the allergen matter inside the tunica mucosa nasi by making an oil film form on the surface of the tunica mucosa nasi further, it found out that said purpose could be attained and this invention was completed. That is, this invention is a rhinenchysis agent which consists of an O/W mold emulsion of pH 3.5-5.5.

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by powerful shearing force, such as a homomixer, MANTON gaulin, and an ultrasonic emulsifier, in that case.

EXAMPLE

[Example] An example and the example of a trial are shown below, and this invention is further explained to a detail.
The example 1 (manifestation trial of the nasal allergy symptom by the rhinenchysis agent) of a trial
[Preparation of a sample]
Sample 1: 0.02 % of the weight of benzethonium chloride, vitamin C 0.5% of the weight, melt 1.5 % of the weight of glycerols to purified water, and carry out churning mixing, the thing which made the surface active agent dissolve HCO-60 (trade name of polyoxyethylene hydrogenated castor oil 60) 0.2 % of the weight and RESHINORU S-10 (trade name of hydrogenation soybean lecithin) 0.5 % of the weight to PANASETO 810 (trade name of medium-chain-fatty-acid triglyceride) 20% of the weight is made to emulsify, the dilute hydrochloric acid of pH regulator is set to pH4 of ** for optimum dose, and pharmaceutical preparation, and it ****s in the 100g of whole quantity.
Sample 2: Phosphate buffer solution (pH7.8).
[0011] [Test.method] An oral consultation was given about 15 23-42-year-old allergic rhinitis patients, and it checked that it was pollinosis. The duration of test could be two weeks. It divided into two groups of A; 8 persons and B; 7 persons, and one week of the start did not perform nasal cavity washing, but followup of the symptom only by the nasal drop was performed. the following one week -- A group; -- a sample 1 and B group; -- spraying administration of the sample 2 was carried out by a unit of 2 times before the time of going home, and sleeping after lunch at both nasal cavities at the time of morning rising. The judgment according extent of the allergy symptom on the 1st to self-assessment was performed, and the symptom log vote was filled in. Throughout [trial term] stopped use of the sinus medication by oral administration. Moreover, concomitant use of the commercial collunarium was accepted if needed for a symptom. I had the use count of the rhinenchysis indicated on a case card in that case.
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[0013]
[Table 1]

年齢	性	観察日　第1週目													
		1日目		2日目		3日目		4日目		5日目		6日目		7日目	
		程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数
A群															
23	女	++	13	++	10	+++	16	++	7	++	10	++	15	+++	15
25	女	++	14	++	12	++	11	++	13	+++	16	++	10	++	12
26	男	++	7	++	6	++	8	++	8	++	8	++	7	++	6
27	女	++	5	++	5	+	4	+	6	+	7	+	8	++	10
28	男	+	6	+	6	+	6	+	6	+	7	+	8	+	7
28	男	++	7	+	7	+	8	++	10	++	10	+	7	+	6
36	男	++	10	++	10	+++	13	+++	14	++	12	++	10	+++	13
42	男	++	7	++	9	++	8	++	8	++	8	++	10	+	6
B群															
24	男	++	15	+++	15	++	10	++	12	+++	13	+++	10	+++	14
24	女	+	8	+	9	+	7	+	5	++	13	+	8	++	15
26	女	++	15	+++	20	++	18	+++	22	+++	20	+++	23	+++	20
27	女	+	7	+	7	+	8	+	6	+	7	+	5	+	7
29	男	++	10	++	8	+	9	+++	11	+++	11	+++	12	+++	14
33	男	++	10	++	7	++	8	+	5	+	10	++	10	++	13
36	男	++	11	++	11	++	11	++	9	++	8	++	10	++	15

症状の程度：4段階

高　度（非常に悪い）：+++

中等度（　　悪い）：++

軽度　（　やや悪い）：+

なし　（　　良好）：−

[0014]

[Table 2]

年齢	性	観察日　第２週目													
		１日目		２日目		３日目		４日目		５日目		６日目		７日目	
		程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数	程度	回数
A群															
２３	女	＋＋	7	＋	5	＋＋	6	＋	5	＋	6	＋＋	9	＋	7
２５	女	＋＋	8	＋	4	＋	5	＋＋	5	＋	5	＋＋	7	＋＋	6
２６	男	＋＋	7	＋	5	＋	5	＋＋	6	＋＋	6	＋＋	5	＋＋	5
２７	女	＋＋	5	＋＋	5	＋	4	＋	4	＋＋	5	＋	4	＋	5
２８	男	＋	6	＋	6	＋	6	＋	5	＋	4	＋	4	＋	5
２８	男	＋＋	7	＋＋	8	＋＋	7	＋	6	＋	6	＋＋	7	＋＋	7
３６	男	＋＋	10	＋＋	10	＋＋	10	＋＋	8	＋＋	10	＋＋	11	＋＋	10
４２	男	＋＋	8	＋＋	7	＋＋	7	＋	6	＋	6	＋	5	＋	6
B群															
２４	男	＋＋	10	＋＋	12	＋＋＋	13	＋＋	11	＋＋	9	＋＋	8	＋＋＋	13
２４	女	＋＋	10	＋	5	＋	8	＋＋	11	＋＋	12	＋＋	10	＋＋	10
２６	女	＋＋＋	20	＋＋＋	25	＋＋＋	18	＋＋＋	18	＋＋＋	20	＋＋＋	20	＋＋＋	18
２７	女	＋	7	＋	5	＋＋	10	＋	6	＋	4	＋＋	8	＋	4
２９	男	＋＋	10	＋＋	9	＋＋＋	14	＋＋＋	14	＋＋	10	＋＋	8	＋＋	8
３３	男	＋＋	8	＋＋	7	＋＋	10	＋＋＋	15	＋＋＋	15	＋＋	10	＋＋	10
３６	男	＋＋	8	＋＋	10	＋＋	10	＋＋	10	＋＋＋	15	＋＋	10	＋	9

症状の程度：４段階

高　度（非常に悪い）：＋＋＋

中等度（　　悪い）：＋＋

軽度　（　やや悪い）：＋

なし　（　　良好）：－

[0015] Example 1 Component Loadings (% of the weight)
Benzethonium chloride 0.02 PANASETO 810 30 RESHINORU S-10 0.5 Glycerol 2 L-menthol 0.05 Dilute hydrochloric acid Optimum dose (pharmaceutical preparation pH 4.5)
Purified water All 100g benzethonium chloride and a glycerol were melted to purified water, and the rhinenchysis agent was prepared by carrying out churning mixing, making what dissolved HCO-60, RESHINORU S-10, and l-menthol in PANASETO 810 emulsify, setting dilute hydrochloric acid to pH4 of ** for optimum dose, and pharmaceutical preparation, and considering as 100g of whole quantity.
[0016] Example 2 Component Loadings (% of the weight)
Lidocaine 0.1 Benzethonium chloride 0.02 PANASETO 810 10 HCO-60 0.2 RESHINORU S-10 0.3 Glycerol 1.5 Hydroxymethyl cellulose 0.02 Phosphate buffer solution A total (pharmaceutical preparation pH 3.5) of 100g
The rhinenchysis agent was substantially prepared similarly with the example 1.
[0017] Example 3 Component Loadings (% of the weight)
Cetylpyridinium chloride 0.02 Soybean oil 20 Tween80 0.2 RESHINORU S-10 0.5 Glycerol 1.0 Dilute hydrochloric acid Optimum dose (pharmaceutical preparation pH 5.0)
Purified water The rhinenchysis agent was substantially prepared similarly with all the 100g examples 1.

[0018] Example 4 Component Loadings (% of the weight)
Glycyrrhizinate dipotassium 0.5 Benzethonium chloride 0.02 PANASETO 810 10 HCO-60 0.2 RESHINORU S-10 0.3 Glycerol 1.5 Hydroxymethyl cellulose 0.01 Dilute hydrochloric acid Optimum dose (pharmaceutical preparation pH 4.0) Purified water The rhinenchysis agent was substantially prepared similarly with all the 100g examples 1.
[0019] Example 5 Component Loadings (% of the weight)
Benzalkonium chloride 0.02 PANASETO 810 30 Pre SOMU 0.5 Glycerol 1.5 Phosphate buffer solution A total (pharmaceutical preparation pH 4.0) of 100g The rhinenchysis agent was substantially prepared similarly with the example 1.

CLAIMS

[Claim(s)]
[Claim 1] The rhinenchysis agent which consists of an O/W mold emulsion of pH 3.5-5.5.